Applicant: Breaker et al. U.S. Serial No.: 09/830,905

In the Claims:

. Please cancel claims 8 and 20.

Replace the pending claims with the following:

- 1. (Amended) A purified functional polynucleotide comprising
- (a) an actuator domain comprising at least a fragment of a pre-existing actuator nucleotide sequence,
- (b) a receptor domain comprising at least a fragment of a pre-existing receptor nucleotide sequence, and
- (c) a randomized bridging domain comprising a random nucleotide sequence, wherein interaction of the receptor domain with a signaling agent triggers a conformational change in the randomized bridging domain which modulates the activity of the actuator domain.
- 2. (Amended) A polynucleotide according to claim 1 wherein the signaling agent is a ligand that binds to the receptor domain.
- 3. A polynucleotide according to claim 1 wherein the activity of the actuator domain is catalytic.
- 4. A polynucleotide according to claim 1 wherein at least two of the domains are non-overlapping.

N.E

- 5. A polynucleotide according to claim 1 wherein at least two of the domains are partially or completely overlapping.
- 6. A polynucleotide according to claim 1 which is RNA.
- 7. A polynucleotide according to claim 6 which is a hammerhead ribozyme.

Applicant: Breaker et al. U.S. Serial No.: 09/830,905

- 9. A polynucleotide according to claim 1 wherein the actuator domain exhibits catalytic activity that is triggered by binding of a chemical compound to the receptor domain.
- 10. (Previously Amended) A biosensor comprising a polynucleotide according to claim 1.
- 11. A biosensor according to claim 10 in which the polynucleotide is attached to a solid support.
- (Previously Amended) A method for detecting the presence or absence of a ligand or its concentration in a sample comprising contacting the sample with a polynucleotide according to claim 1.
- A method according to claim 12 wherein the presence or absence of a ligand or its 13. concentration is determined by observation of a chemical reaction.
- 14. A method according to claim 12 wherein the presence or absence of a ligand or its concentration is detected by observation of a change in polynucleotide configuration or function.

(Amended) A process for preparing polynucleotides that are responsive to the presence or

absence of a signaling agent, comprising linking together a polynucleotide actuator domain

15.

- comprising at least a fragment of a pre-existing actuator nucleotide sequence, a receptor domain comprising at least a fragment of a pre-existing receptor nucleotide sequence, and a randomized bridging domain comprising a random nucleotide sequence, such that interaction of the signaling agent with the receptor domain triggers a conformational change in the randomized bridging domain which modulates the activity of the actuator domain.
- 16. A process according to claim 15 wherein the receptor domain has a ligand binding site and wherein ligand binding triggers a conformational change in the bridging domain that stimulates catalytic activity of the actuator domain.

17. (Amended) A process for screening polynucleotides which have an actuator domain, a receptor domain, and a randomized bridging domain and which are responsive to a signaling agent in a sample, comprising linking a randomized bridging domain comprising a random nucleotide sequence and having defined properties that modulate the activity of a corresponding actuator domain having defined properties and comprising at least a fragment of a pre-existing actuator nucleotide sequence, to a receptor domain having a random sequence, and identifying polynucleotides responsive to the signaling agent by incubating the sample with the polynucleotide so constructed and by observing modulation of the activity of the actuator domain.



18. (Amended) A process according to claim 17 wherein the receptor domain has a ligand binding site and wherein ligand binding triggers a conformational change in the randomized bridging domain that stimulates catalytic activity of the actuator domain.



19. (Previously Amended) A process for preparing RNA sensors according to claim 15.